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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/509,366	09/24/2004	Sun-Chang Kim	06181/0201899-US0	3993

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EXAMINER	
MOHAMED, ABDEL A	
ART UNIT	**PAPER NUMBER**
1654	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/30/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/509,366	KIM ET AL.	
	Examiner	Art Unit	
	Abdel A. Mohamed	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5,6,10,11,14,15,19 and 20* is/are pending in the application.

4a) Of the above claim(s) *19 and 20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5,6,10,11,14 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 September 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/24/04, 6/9/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

ACKNOWLEDGMENT TO PRIORITY, IDS, AMENDMENT, RESPONSE TO THE RESTRICTION REQUIREMENT, STATUS OF THE APPLICATION AND CLAIMS

1. This application is filed under 35 U.S.C. 371 on 09/24/04 having a filing date of 03/26/03 of PCT/KR03/00602. Acknowledgement is made of Applicant's claim for priority based on Republic of Korea Application No. 10-2002-0016445 having a filing date of 03/26/02. Receipt is acknowledged of papers submitted under 35 U.S.C. § 119, which papers have been placed of record in the file. The information disclosure statements (IDS) and Form PTO-1449 filed 09/24/04 and 06/09/05, the amendment and response to restriction requirement filed 03/12/07, respectively are acknowledged, entered and considered. In view of Applicant's request claims 2, 10, 11, 14 and 15 have been amended; claims 3, 4, 7-9, 12, 13 and 16-18 have been canceled and claim 19 and 20 have been added. Claims 1, 2, 5, 6, 10, 11, 14, 15 19 and 20 are now pending in the application.

OBJECTION TO THE SPECIFICATION

2. The continuity data of this application should be updated in the specification. The disclosure is also objected to because of the following informalities: The description under Brief Description of the Drawings for Figures 1A-1D (page 10) reference colors (photographs obtained by confocal) which distinguishes various results of analyzing the cell penetration activity of antimicrobial peptides by confocal microscopy. However, the drawings are in black and white and thus the description is not consistent with the actual drawings. Appropriate correction is required.

OBJECTION TO THE CLAIMS

3. Claim 2 and claims dependent thereof (i.e., claims 6, 11 and 15) are objected in the recitation the "SEQ ID NOS: 1-34" because the elected sequence is SEQ ID NO:1. Limiting the claim to recite the elected sequence (i.e., SEQ ID NO:1) would obviate this objection.

ELECTION WITH TRAVERSE

4. Applicant's election with traverse of Group I (claims 1, 2, 5, 6, 10, 11, 14 and 15) in the communication filed 03/12/07 is acknowledged. The traversal is on the ground(s) that a portion of Invention Group III shares inventive scope with Invention Group I. SEQ ID NOS:69 and 70, assigned to Invention Group III, have the same amino acid sequences as SEQ ID NOS:16 and 32, but are not C-terminal amidated. SEQ ID NOS:16 and 32 are recited in claim 6, which is assigned to Invention Group I. Therefore, SEQ ID NOS:69 and 70 are also encompassed within the scope of Invention Group I. Thus, the Examiner assign new claims 19 and 20, which call for SEQ ID NOS:69 and 70, to Invention Group I. Applicant concludes by contending that Invention Group I is provisionally elected, and **species** SEQ ID NO:1 is elected for the purpose of searching is noted.

Contrary to Applicant's contention, as stated on page 3 in the previous Office action, the Examiner has clearly indicated with respect to the various sequences recited in Groups I-III, the sequences encompass peptides having different structures which are distinct from each other, and as such, they are considered as patentably distinct and/or

independent, one from the other, and capable of independent use. Further, there is no sequence linking each with other, it is only consensus. Hence, Applicant is required to elect a single disclosed sequence and/or provide a single subsequence within a disclosed sequence wherein the subsequence for the elected is searched.

Thus, the sequences are patentably distinct because they are unrelated sequences and each unrelated sequence is considered a separate and distinct product, therefore a further restriction is applied to each sequence. For an elected invention drawn to either amino acid or polypeptide sequences, the Applicant must further elect a **single** amino acid or a **single** polypeptide sequence (See MPEP 803.04). Due to the increasing large size of sequence databases which must be searched and the increasing numbers of applications requiring sequence searches, it creates an undue burden on the Office to search more than a single sequence (product) per application. For these reasons, the requirement of 37 CFR 1.141 *et seq.* is no longer waived and Applicant is required to elect a **single** sequence for examination. Applicant is reminded that this is a **restriction requirement**, not an election of species as contended by Applicant.

Therefore, since Applicant has elected SEQ ID NO:1, the elected **single** SEQ ID NO:1 will be examined along the elected Group I (claims 1, 2, 5, 6, 10,11, 14 and 15) . Thus, since the various sequences disclosed do not share the same specific technical features, the invention (i.e., the sequences) do not relate to a single inventive concept. Therefore, claims 19 and 20 are withdrawn as non-elected inventions for the reasons of record. Hence, the Office action is directed to the merits of claims 1, 2, 5, 6, 10, 11, 14

and 15 along **SEQ ID NO:1** as *per* elected invention and Applicant is advised to cancel non-elected invention of claims 19 and 20 and SEQ ID NOS:2-34 in the next communication.

The requirement is still deemed proper and is therefore made FINAL.

CLAIMS REJECTION-35 U.S.C. § 102(b)

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) The invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 5, 6, 10, 11, 14 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Kim et al (U.S. Patent No. 5,936,063).

The instantly claimed invention as drafted in claims 1, 2, 5, 6, 10, 11, 14 and 15 are broadly directed to an antimicrobial peptide including the amino acid sequence represented as sequence equation I (claim 1, i.e., any antimicrobial peptide which is not defined, and as such would read on antimicrobial peptide isolated from *Bufo bufo gargarizans*, wherein one of the amino acid sequence is selected from SECID NO:1 (claim 2), wherein the C-terminus of the amino acid sequence is amidated (claims 5 and 6) and wherein the antimicrobial composition comprising at least one antimicrobial peptide as effective ingredient in a pharmaceutically effective amount thereof (claims 10, 11, 14 and 15). The prior art of Kim et al ('063 patent) discloses an antimicrobial peptide isolated from *Bufo bufo gargarizans* exhibiting therapeutic antibacterial and

antifungal properties. To the extent that the antimicrobial peptide is in a physiological buffer it is considered to be a pharmaceutical composition.

Further, the claims are broadly directed to antimicrobial peptides including the amino acid sequence represented as the sequence equation (I). The term "**including**" the amino acid sequence represented as equation (I) will be understood to imply the inclusion of stated element or integer or group of elements or integers but not the exclusion of any other element or integer or group of elements or integers. Thus, the '063 patent clearly discloses a pharmaceutical formulation **comprising** at least one antimicrobial peptide as effective ingredient in a pharmaceutically effective amount.

The Examiner acknowledges that the prior art does not teach the amidation of the C-terminus of amino acid sequence, however, as admittedly acknowledged on pages 4 and 7 in the instant specification, it is within the skill of the art to which this invention pertains to synthesize amino acids of interest by substituting, adding or deleting or exchanging the residues at N-terminus and C-terminus thereby selecting repeatedly the peptide analogs which is able to penetrate into microbial cells and act against the microorganisms by exhibiting antimicrobial activities. Therefore, in view of the above and in view the claims languages "**including**" and "**comprising**" which would not exclude antimicrobial peptide isolated from *Bufo bufo gargarizans*, the prior art teachings clearly encompasses the antimicrobial fragments claimed as amino acid sequence represented as sequence equation (I) and as SEQ ID NO:1, in the absence of evidence to the contrary, the claimed antimicrobial peptide comprising a pharmaceutical

formulation thereof disclosed by the reference anticipates claims 1,2, 5, 6, 10, 11, 14 and 15 as drafted.

6. Claims 1, 2, 5, 6, 10, 11, 14 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Park et al (Biological and Biophysical research Communications, Vol. 244, pp. 253-257, 1998).

The instantly claimed invention as drafted in claims 1, 2, 5, 6, 10, 11, 14 and 15 are broadly directed to an antimicrobial peptide including the amino acid sequence represented as sequence equation I (claim 1, i.e., any antimicrobial peptide which is not defined, and as such would read on antimicrobial peptide isolated from *Bufo bufo gargarizans*, wherein one of the amino acid sequence is selected from SECID NO:1 (claim 2), wherein the C-terminus of the amino acid sequence is amidated (claims 5 and 6) and wherein the antimicrobial composition comprising at least one antimicrobial peptide as effective ingredient in a pharmaceutically effective amount thereof (claims 10, 11, 14 and 15). The prior art of Park et al discloses the isolation of a 39-amino acid peptide buforin I from the stomach tissue of the Asian toad *Bufo bufo gargarizans*, and a more potent buforin II consisting of 21 amino acids was derived from buforin I. Buforin II showed a strong antimicrobial activity against a broad spectrum of microorganism, including Gram-positive and Gram-negative bacteria, as well as fungi without any significant hemolytic activity. To the extent that the antimicrobial peptide is in a physiological buffer it is considered to be a pharmaceutical composition.

Further, the claims are broadly directed to antimicrobial peptides including the amino acid sequence represented as the sequence equation (I). The term "**including**" the amino acid sequence represented as equation (I) will be understood to imply the inclusion of stated element or integer or group of elements or integers but not the exclusion of any other element or integer or group of elements or integers. Thus, the '063 patent clearly discloses a pharmaceutical formulation **comprising** at least one antimicrobial peptide as effective ingredient in a pharmaceutically effective amount.

The Examiner acknowledges that the prior art does not teach the amidation of the C-terminus of amino acid sequence, however, as admittedly acknowledged on pages 4 and 7 in the instant specification, it is within the skill of the art to which this invention pertains to synthesize amino acids of interest by substituting, adding or deleting or exchanging the residues at N-terminus and C-terminus thereby selecting repeatedly the peptide analogs which is able to penetrate into microbial cells and act against the microorganisms by exhibiting antimicrobial activities. Therefore, in view of the above and in view the claims languages "**including**" and "**comprising**" which would not exclude antimicrobial peptide isolated from *Bufo bufo gargarizans*, the prior art teachings clearly encompasses the antimicrobial fragments claimed as amino acid sequence represented as sequence equation (I) and as SEQ ID NO:1, in the absence of evidence to the contrary, the claimed antimicrobial peptide comprising a pharmaceutical formulation thereof disclosed by the reference anticipates claims 1,2, 5, 6, 10, 11, 14 and 15 as drafted.

7. Claims 1, 2, 5, 6, 10, 11, 14 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Park et al (PNAS, USA, Vol. 97, No. 15, pp 8245-8250, July 19, 2000).

The instantly claimed invention as drafted in claims 1, 2, 5, 6, 10, 11, 14 and 15 are broadly directed to an antimicrobial peptide including the amino acid sequence represented as sequence equation I (claim 1, i.e., any antimicrobial peptide which is not defined, and as such would read on antimicrobial peptide isolated from *Bufo bufo gargarizans*, wherein one of the amino acid sequence is selected from SECID NO:1 (claim 2), wherein the C-terminus of the amino acid sequence is amidated (claims 5 and 6) and wherein the antimicrobial composition comprising at least one antimicrobial peptide as effective ingredient in a pharmaceutically effective amount thereof (claims 10, 11, 14 and 15). The prior art of Park et al discloses the isolation of a 39-amino acid peptide buforin I from the stomach tissue of the Asian toad *Bufo bufo gargarizans*, and a more potent antimicrobial peptide of 21 amino acids, called buforin II was derived from buforin I. Buforin II shows much stronger antimicrobial activity against a broad-spectrum microorganisms thus exhibiting therapeutic antibacterial and antifungal properties. To the extent that the antimicrobial peptide is in a physiological buffer it is considered to be a pharmaceutical composition.

Further, the claims are broadly directed to antimicrobial peptides including the amino acid sequence represented as the sequence equation (I). The term "**including**" the amino acid sequence represented as equation (I) will be understood to imply the inclusion of stated element or integer or group of elements or integers but not the exclusion of any other element or integer or group of elements or integers. Thus, the

reference of Park et al clearly discloses a pharmaceutical formulation **comprising** at least one antimicrobial peptide as effective ingredient in a pharmaceutically effective amount.

With respect to the amidation of the C-terminus of amino acid sequence as claimed in claims 5 and 6, the prior art clearly discloses the amidation of C-terminus by stating that to elucidate the structural features of buforin II that are required for its potent antimicrobial activity, we synthesized a series of N- and C-terminally truncated or amino acid-substituted synthetic buforin II analogs and examined their antimicrobial activity and mechanism of action (See e.g., abstract). Furthermore, as admittedly acknowledged on pages 4 and 7 in the instant specification, it is within the skill of the art to which this invention pertains to synthesize amino acids of interest by substituting, adding or deleting or exchanging the residues at N-terminus and C-terminus thereby selecting repeatedly the peptide analogs which is able to penetrate into microbial cells and act against the microorganisms by exhibiting antimicrobial activities. Therefore, in view of the above and in view the claims languages "**including**" and "**comprising**" which would not exclude antimicrobial peptide isolated from *Bufo bufo gargarizans*, particularly buforin II, the prior art teachings clearly encompasses the antimicrobial fragments claimed as amino acid sequence represented as sequence equation (I) and as SEQ ID NO:1, in the absence of evidence to the contrary, the claimed antimicrobial peptide comprising a pharmaceutical formulation thereof disclosed by the reference anticipates claims 1,2, 5, 6, 10, 11, 14 and 15 as drafted.

CITATION OF RELEVANT PRIOR ART

8. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. WO 99/37664 discloses the development of antimicrobial peptides that have an enhanced antimicrobial activities and are not sensitive to salt concentration to have antimicrobial activities *in vivo*.

Park et al (The Journal of Biological Biochemistry, Vol. 279, No. 14, pp. 13896-13901, April 12, 2004) disclose results which indicate that antimicrobial peptides provides the necessary structural stability for the peptides to permeabilize cell membranes and cause cell death at physiological salt concentrations.

CONCLUSION AND FUTURE CORRESPONDANCE

9. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed whose telephone number is (571) 272 0955. The examiner can normally be reached on First Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tsang Cecilia can be reached on (571) 272 0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

AAM Mohamed/AAM
April 23, 2007.

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